Australia-based Phase 1 Trial of a Novel, Hydrogel-based, Intravitreal Axitinib Implant for the Treatment of Neovascular Age-related Macular Degeneration

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Disclosures

- **Presenter:**
  - *Consulting*: Allergan, Genentech, Graybug, Novartis, Ocular Therapeutix, Placid0, Pr3vent, Regeneron, RegenXBio
  - *Research Grants*: Genentech, Novartis, Regeneron
  - *Equity Interests*: OptiSTENT, Ocular Therapeutix, Placid0, Pr3vent
- **Study Disclosures:** This clinical trial was sponsored by Ocular Therapeutix, Inc.

The following presentation discusses an investigational drug, OTX-TKI, in development. OTX-TKI's efficacy and safety profiles have not been established, and it has not been approved for marketing by the FDA.

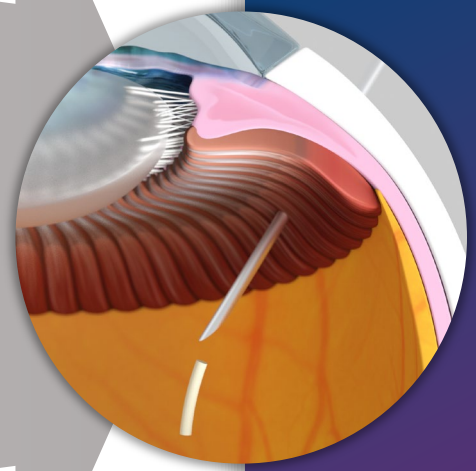
OTX-TKI: Axitinib in a Bioresorbable Hydrogel Implant

Axitinib
(Active Ingredient)

- Highly selective inhibitor of all VEGF and PDGF receptors[1,2]
- High affinity and low solubility compared to other TKIs being investigated for nAMD[2,3]

Polyethylene Glycol
(PEG)-based Hydrogel Platform[4]

- Demonstrated biocompatibility with low potential for inflammation
- Highly programmable bioresorption



OTX-TKI
Axitinib in an Intravitreal Hydrogel Implant

- Single implant designed to deliver axitinib for 6-9 months
- Bioresorbs completely and is cleared from the vitreous
- Delivered through 25-gauge needle or smaller

References: 1. Zhao Y, et al. *Oncologist*. 2015;20(6):660-673. **2.** Gross-Goupil M, et al. *Clin Med Insights Oncol*. 2013;7:269-277. **3.** Eyepoint Pharmaceuticals, Inc. Form 8-K. Published online September 15, 2020. Accessed August 24, 2022. https://sec.report/Document/0001564590-20-043596/ **4.** Sawhney AS, et la. US patent 8,409,606 B2. April 2, 3013.
Abbreviations: nAMD, neovascular age-related macular degeneration; PDGF, platelet derived growth factor; TKI, tyrosine kinase inhibitor; VEGF, vascular endothelial growth factor

OTX-TKI Phase 1 Trial in Australia

Research Question: Does axitinib (tyrosine kinase inhibitor) have biological activity in wet AMD subjects with retinal fluid when administered intravitreally?

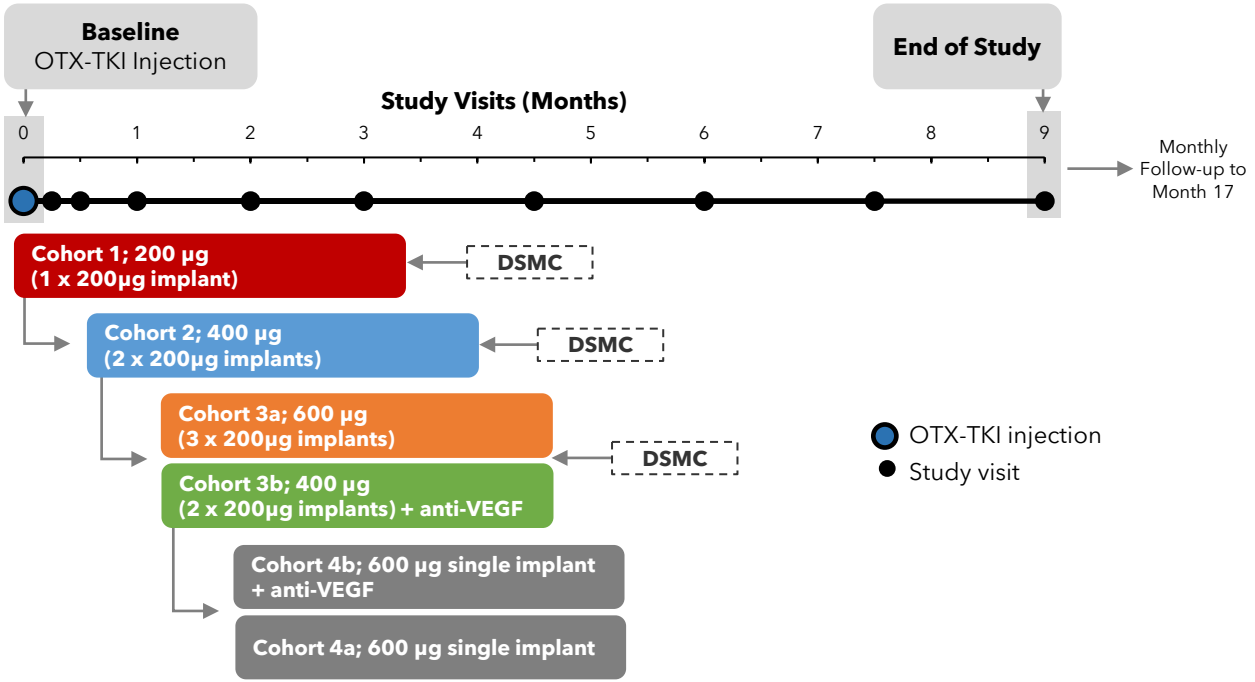
Open-label, Dose Escalation, Feasibility Trial

Objectives

- Safety and tolerability
- Biological activity: mean change in central subfield thickness measured by SD-OCT, BCVA, and clinically-significant leakage on FA and/or OCT-A

Key Inclusion Criteria

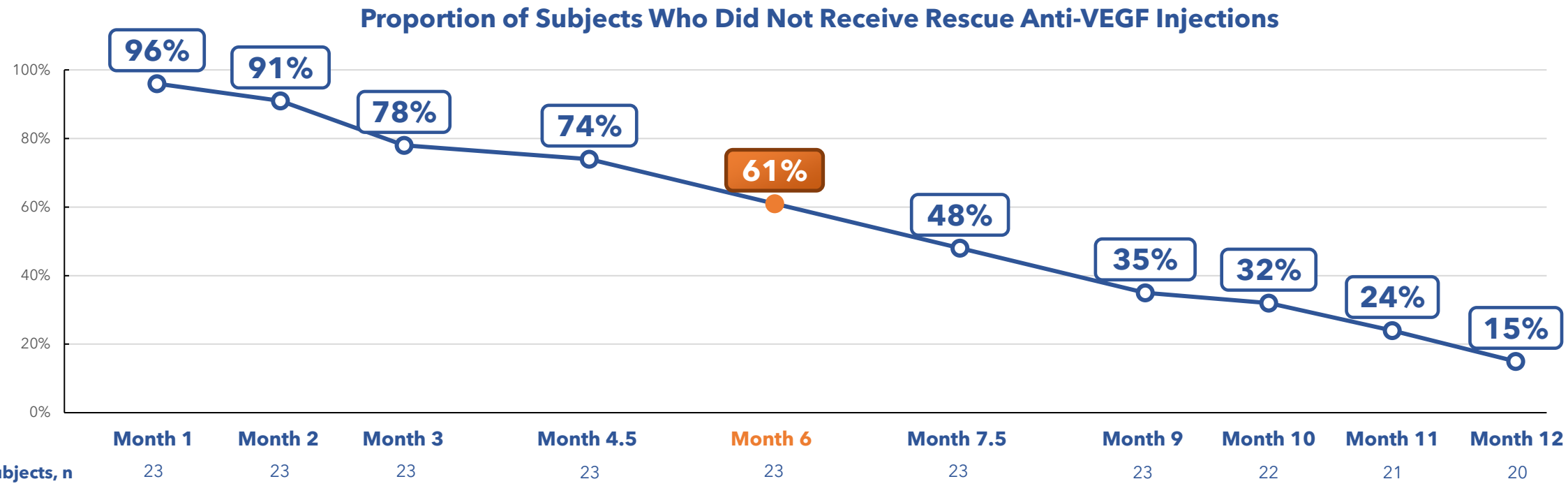
- Active primary sub foveal neovascularization secondary to AMD
- **Previously treated or treatment naïve subjects**
- **Presence of retinal fluid**



Abbreviations: AMD, age-related macular degeneration; BCVA, best corrected visual acuity; DSMC, data and safety monitoring committee; FA, fluorescein angiography; OCT-A, optical coherence tomography angiography; SD-OCT, spectral domain optical coherence tomography

Rescue-Free Rates: All Subjects

Over ~60% of all subjects did not receive anti-VEGF rescue injections for 6 months



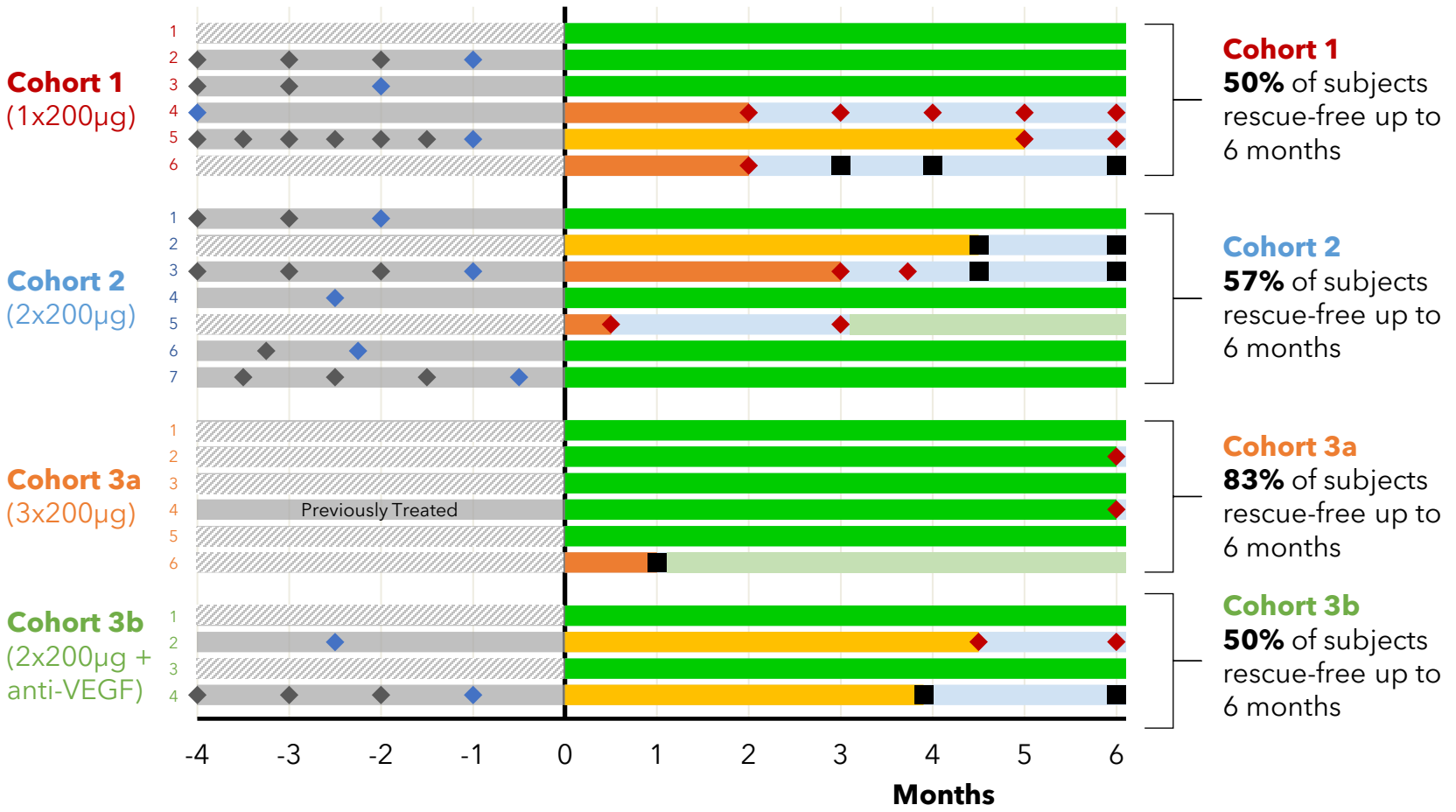
Rescue Criteria:

- **If needed, any subject in any treatment arm may receive rescue therapy (i.e., anti-VEGF) at the investigator's discretion regardless of meeting rescue criteria**
- The following criteria were used to identify subjects who will likely require rescue therapy: 1) loss of ≥15 letters from best previous BCVA due to AMD, with current BCVA not better than baseline; or 2) loss of ≥10 letters on 2 consecutive visits from best previous BCVA due to AMD, with current BCVA score not better than baseline; or 3) evidence of worsening disease activity manifest by >75 microns CSFT from previous best value

NOTE: Interim review, unmonitored data; Data cut off August 5, 2022

OTX-TKI Durability

After treatment with OTX-TKI, median time to first rescue with anti-VEGF was 7 months



Cohort 1
50% of subjects rescue-free up to 6 months

Cohort 2
57% of subjects rescue-free up to 6 months

Cohort 3a
83% of subjects rescue-free up to 6 months

Cohort 3b
50% of subjects rescue-free up to 6 months

Treatment Status
- Treatment Naive
- Previously Treated

Time to First Rescue
- ≥6 months
- 4 to 5 months
- ≤3 months

Time After Rescue
- After first rescue
- >6 months after rescue

Anti-VEGF Injections
- Rescue injection - Rescue criteria met
- Rescue injection given at investigator's discretion (rescue criteria **not met**)
- Anti-VEGF injections prior to OTX-TKI treatment (estimated)
- Last anti-VEGF injection prior to OTX-TKI treatment (actual)
- Hydrogel implant(s) and drug no longer visible

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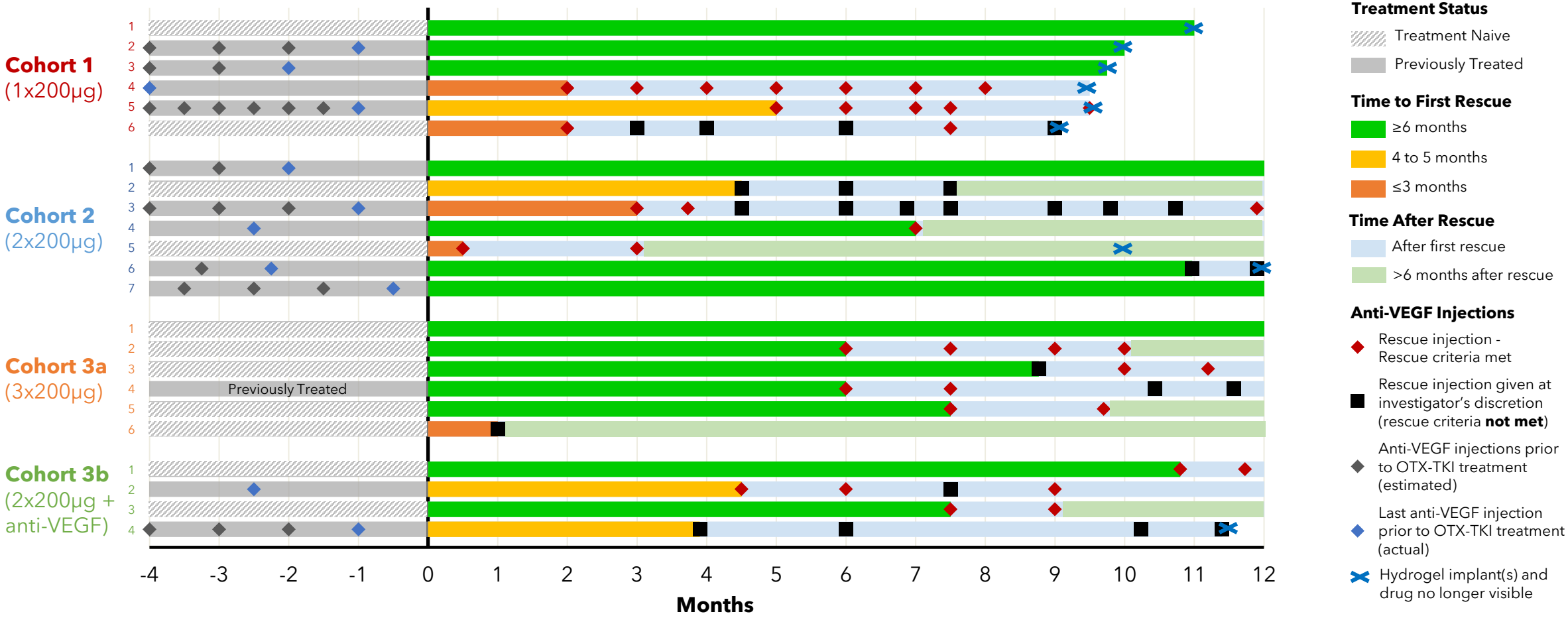
OTX-TKI Durability

After treatment with OTX-TKI, median time to first rescue with anti-VEGF was 7 months



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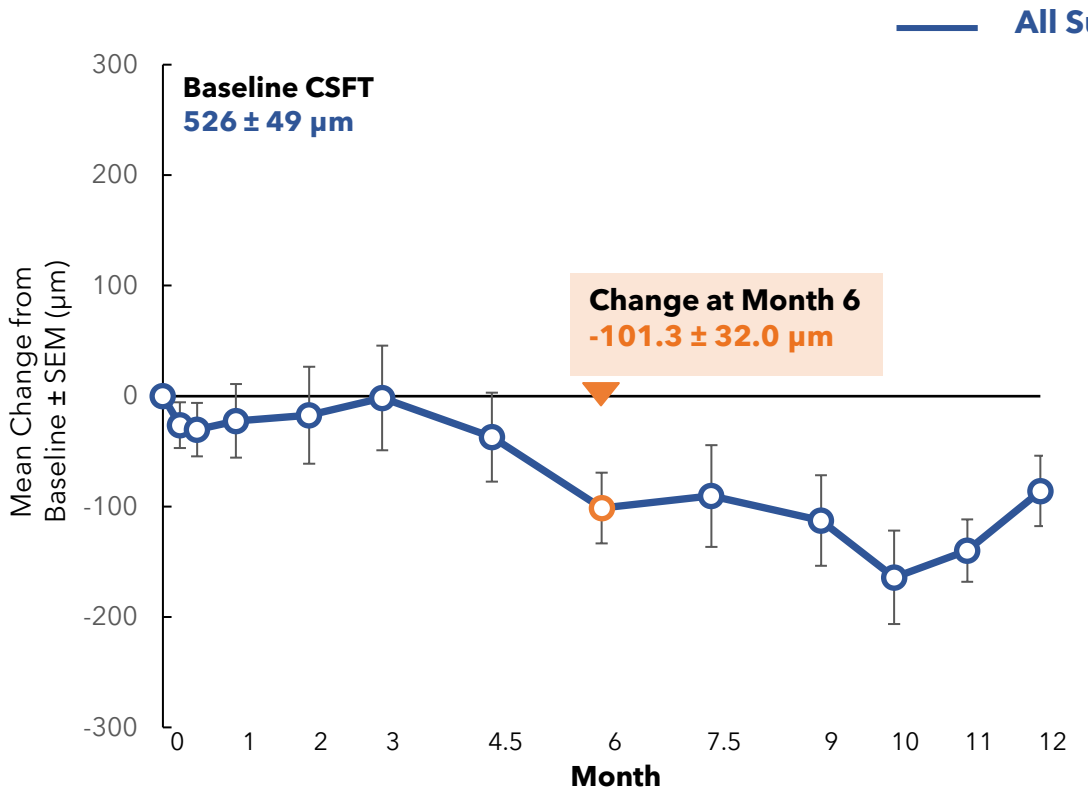
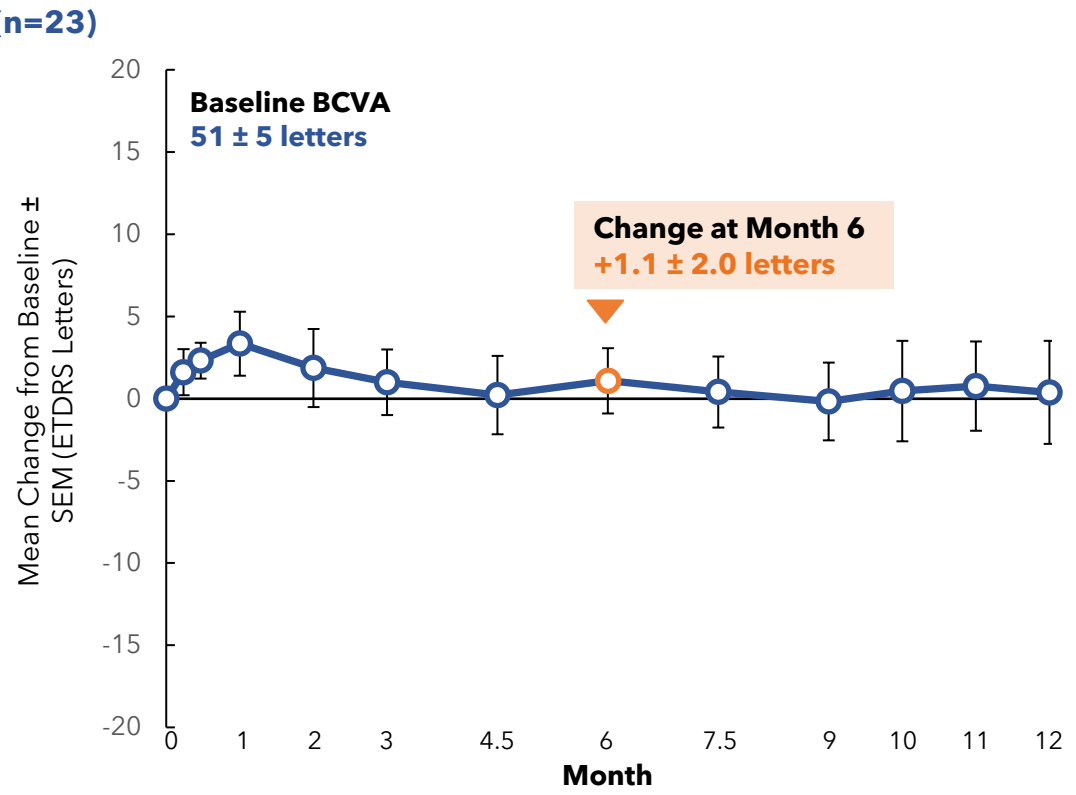
CSFT and BCVA: All Subjects

Effective control of retinal fluid and vision demonstrating sustained activity over time

Central Subfield Thickness (CSFT)



Best Corrected Visual Acuity (BCVA)



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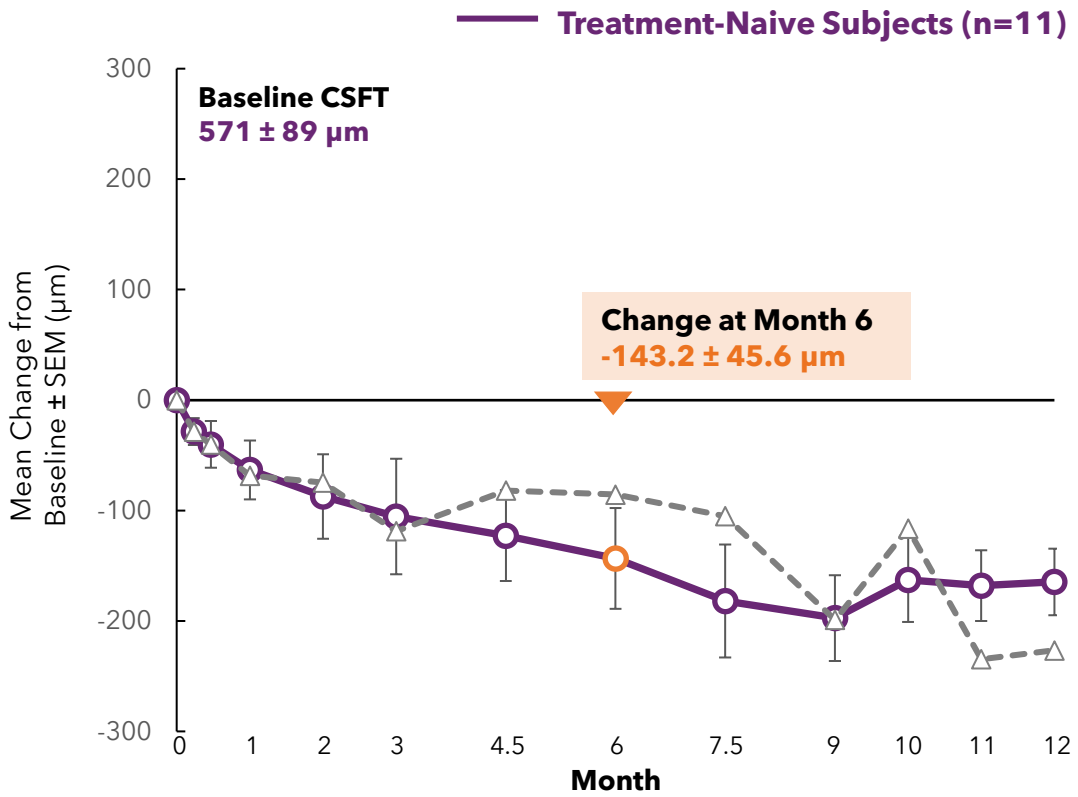
CSFT and BCVA: Treatment Naïve Subjects

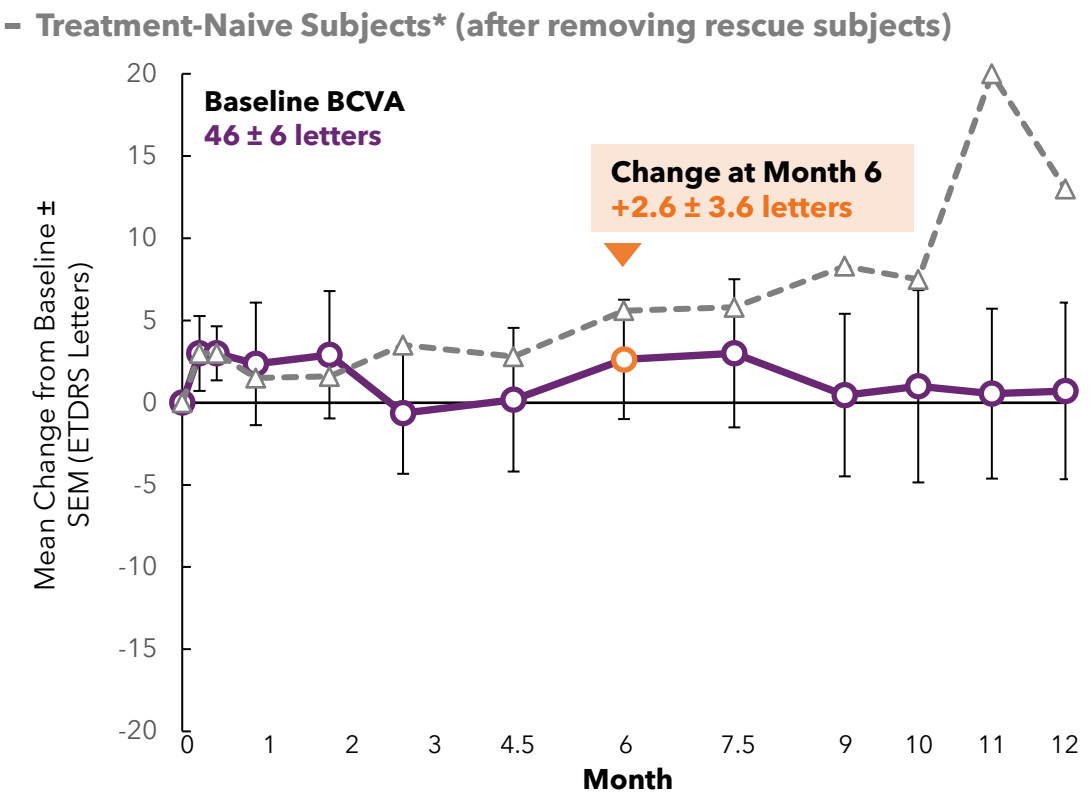
Evidence of biological activity observed after single treatment with OTX-TKI

Central Subfield Thickness (CSFT)



Naïve Subjects, n	11	11	11	11	11	10	10	11	7	9	6
Naïve Subjects after removing rescue , n	11	10	9	8	8	6	5	3	2	1	1

Best Corrected Visual Acuity (BCVA)



Naïve Subjects, n	11	11	11	11	11	11	10	11	8	9	7
Naïve Subjects after removing rescue, n	11	10	9	8	8	6	5	3	2	1	1

NOTE: Interim review, unmonitored data; Data cut off August 5, 2022
Number of treatment-naïve subjects in each cohort. Cohort 1 (n=2), Cohort 2 (n=2), Cohort 3a (n=5), and Cohort 3b (n=2)

Safety and Tolerability

No serious ocular adverse events reported

No reports of significant adverse events:

- No endophthalmitis
- No retinal detachment
- No implant migration into the anterior chamber
- No elevated IOP
- No retinal vasculitis

Adverse Events in the Study Eye	Cohort 1 200 µg n=6	Cohort 2* 400 µg n=7	Cohort 3a* 600 µg n=6	Cohort 3b* 400 µg + anti-VEGF n=4	Total n=23
Vitreous floaters	0	1	0	2	3
Endophthalmitis	0	0	0	0	0
Retinal detachment	0	0	0	0	0
Implant migration into AC	0	0	0	0	0
Elevated IOP	0	0	0	0	0
Ocular inflammation	0	0	0	1	1
Adverse Events Reported in >2 Subjects					
Subconjunctival hemorrhage	1	3	5	4	13
Eye pain	0	2	2	0	4
Worsening cataract	0	1	2	1	4
Pigmented keratic precipitates	3	0	0	0	3
Dry eye	1	0	1	1	3

Follow-up is ongoing
NOTE: Interim review, unmonitored data; Data cut off August 5, 2022

Summary of Interim Data from OTX-TKI Phase 1 Australia Study

Safety to Date

- OTX-TKI was well tolerated and had a favorable safety profile
- No ocular serious adverse events observed

Preliminary Biological Activity Observed

- On average, stable to improved vision with reduced retinal thickness
- Treatment naïve patients with improved retinal fluid and visual acuity without anti-VEGF

Durability Data Suggests Extended Duration of Action

- Overall, 60% of subjects did not require rescue at 6 months
- 83% of Cohort 3a (highest dose) reached month 6 without receiving rescue injection

Implant Monitoring

- A single implant was observed to be bioresorbed by 9 to 10.5 months with limited movement after implantation
- No implant migration observed

Proof of concept of TKI efficacy demonstrated in treatment naïve patients with OTX-TKI

NOTE: Interim review, unmonitored data; Data cut off August 5, 2022

U.S Phase 1 Trial

7 Month Analysis is available at AAO 2022 On-Demand Poster PO359

Key Inclusion Criteria

- Sub foveal neovascularization secondary to AMD
- **Previously treated** with anti-VEGF injections and **controlled fluid** per investigator

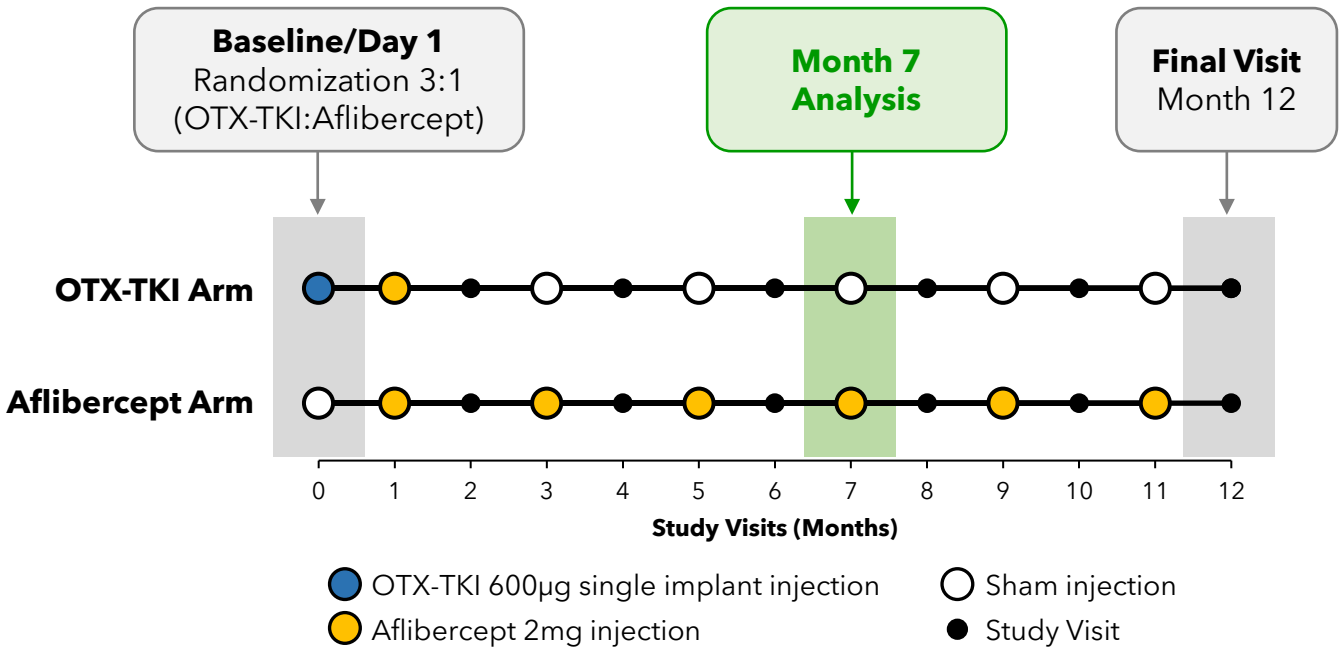
Objectives

- Safety, tolerability, durability and biological activity
- BCVA, mean change in CSFT measured by SD-OCT and safety evaluations

Key Differences in Study Design:

	US Phase 1 Study	Australia Phase 1 Study
Inclusion Criteria	**Controlled fluid**	Presence of retinal fluid
OTX-TKI Implant	**One 0.6 mg (600 µg) single implant**	Cohorts 1-3 used one to three 0.2 mg implants to achieve different doses (0.2, 0.4 and 0.6 mg)
Anti-VEGF Induction	**Yes, all subjects**	Only in Cohort 3b and 4b
Rescue Criteria	**i. Loss of ≥10 letters[a]** **ii. Evidence of >75µm CSFT & ≥5 letters loss[b]** **iii. New macular hemorrhage**	**i. Loss of ≥15 letters[a]** **ii. Loss of ≥10 letters on 2 consecutive visits[a]** **iii. Evidence of >75µm CSFT[b]**

Multicenter, Randomized, Double-masked Trial



[a]From best previous BCVA due to AMD, with current BCVA not better than baseline
[b]Evidence of worsening disease activity manifest by greater than 75 µm CSFT from previous best value; letter loss compared to best previous value
Abbreviations: AMD, age-related macular degeneration; BCVA, best corrected visual acuity; BL, baseline; CSFT, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor